

Acute Findings in an acquired neurosensory syndrome

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Abstract

Background

Beginning in 2016 and continuing into 2017 Personnel and their families stationed in Havana Cuba began to present with symptoms of dizziness, ear pain, and tinnitus. As these symptoms began to appear in more personnel an investigation revealed that these individuals reported that the onset of symptoms began after being exposed to a very focal high frequency noise often associated with a pressure wave. These individuals were referred to the University of Miami for evaluation.

Methods

This is a retrospective review that examines the presenting findings of this group of patients. The review is approved by the IRB at the University of Miami.

Results

All of the symptomatic individuals reported some combination of dizziness/balance difficulty, hearing loss, and difficulty staying focused/slower processing speed, tinnitus, ear pain, and/or headaches. Dizziness (92%) and cognitive complaints (56%) were the most common individual symptoms. All of the 25 affected individuals reported either dizziness or cognitive complaints, with 12/25 (48%) reporting both symptoms. All 25 individuals had at least one objective test abnormality.

Conclusion

This retrospective review focuses on presenting symptoms of a phenomenon that to date has only been described in a group of diplomats from select countries in one location. The preponderance of evidence suggests that symptoms and signs emerge after perception of a localized loud noise or pressure field. At the current time the objective

findings are very similar to findings in mTBI from other sources although some unique features of this exposure pattern have been observed.

Background

Beginning in late 2016 and continuing into 2017 US government personnel and their families stationed in Havana, Cuba began to present to their medical office with complaints of sudden onset dizziness, ear pain, and tinnitus. Medical personnel working in that office as well as US government officials began to investigate this illness in which affected individuals complained of hearing an unexplained noise before the symptoms began. The affected individuals characterized the sound as being 1) Loud, 2) High Frequency, 3) Very localized, and 4) Capable of following them throughout a room. In addition, several individuals reported that if they went outside their front door, the noise immediately stopped. Others reported a sensation of pressure in certain parts of the room that could be relieved by moving a few feet away. In response to the incidents the US governments contacted the University of Miami for help in evaluating this group of patients. The University of Miami was chosen for its proximity to Cuba and because the University had several faculty members with expertise in treating similar illness patterns. After examining the first several cases and facing an increasing number of new cases the University and the federal officials decided that a more comprehensive evaluation program was necessary. In this report, we describe the constellation of symptoms observed among affected individuals in the acute phase after perceived exposure. This report is a retrospective review of this group of patients and is limited by the fact that these individuals were all treated as clinical patients and tests and exams were only ordered if necessitated by the clinical picture. This retrospective review has been approved by the IRB at the University of

Miami as well as the University's HIPPA compliance office. It has also been approved by the IRB at the University of Pittsburgh.

Materials and Methods

With the cooperation and facilitation of the US government, the University of Miami conducted evaluations of all individuals who suspected they were affected by an exposure, as well as a sample of individuals who worked and lived in the same geographic area and denied any exposure. Our group examined over 140 individuals and identified 35 with a history of symptoms and/or exposure that mirrored the injury pattern and symptoms that were reported by the early index cases. These 35 individuals reported that they had either experienced the noise and or a pressure wave or were in the same room at the same time as someone experiencing these phenomena. The remaining individuals (a larger group of over 100 individuals) denied any "exposure" to noise or experiencing a pressure sensation, either personally or as reported by those with whom they lived.

These thirty-five individuals were examined at the University of Miami, Miller School of Medicine approximately 7-60 days after the most recent exposure. There were 21 males and 14 females with an age range of 12-64 years of age (mean: 42.3 \pm 11.3 years). All individuals underwent a comprehensive history and physical examination that included a standard set of history questions, a physical exam targeted to the head and neck, and a neurologic examination. Standard eye movement testing was performed as part of the neurologic exam and this testing

was filmed for more precise computer analysis. Individuals were referred for other tests such as formal neuropsychological testing in accordance with the results of this history and physical. No individual was sent for testing that was not clinically indicated.

Results

The initial exam identified ten individuals (6 male and 4 female) who had no symptoms of an exposure, either while at home in Cuba or during our exam. None of these individual complained of symptoms and their exams were entirely normal. Only two of these asymptomatic individuals reported direct exposure; one reported a sensation of exposure to a force wave and a second heard a very brief, high-pitched noise on a single occasion. The remaining eight unaffected patients reported only indirect exposure, defined as being present in the same room at the time another individual experienced a direct exposure. This group of ten is designated as the 'unaffected group.'

The remaining 25 individuals reported direct exposure and were symptomatic (Table 1). This 'affected group' included 15 males and 10 females with the same age range (12-64 years of age and the same average age as the larger group (Mean 43.2 ± 12.6 years of age).

The affected individuals all reported direct exposure to either noise or pressure. In many cases, their search for the origin of the noise (with the noise following them)

resulted in a more prolonged exposure. A few individuals had briefer, exposures, but these occurred over several nights. The majority initially complained of ear pain (often unilateral), tinnitus, and some unsteadiness starting during or right after exposure. On presentation at our institution, the affected individuals reported a variety of symptoms that could largely be qualified as neurosensory. All of the symptomatic individuals reported some combination: 1) Dizziness/balance difficulty, 2) Hearing loss, 3) Difficulty staying focused and slower processing speed, 4) Tinnitus, 5) Ear pain, and 6) Headaches. The symptom distributions are included in Table 1. Dizziness (23/25, 92%) and cognitive complaints (14/25, 56%) were the most common individual symptoms in the affected group and all of the symptoms except headache were significantly more frequent in the symptomatic patients as compared to the asymptomatic. All of the 25 affected individuals reported either dizziness or cognitive complaints, with 12/25 (48%) reporting both symptoms. In addition, the affected group had a very high incidence of two or more symptoms. All but one of the affected individuals (96%) had two or more symptoms (that one individual only had dizziness). Sixteen individuals (64%) in the affected group had three or more symptoms. Even if headache is excluded 14 patients (56%) in the affected group presented with three or more symptoms.

The covariation between the neuro-otologic symptoms was striking. Fifteen affected individuals reported either tinnitus or hearing loss (both symptoms reported by only one person), while 14 affected individuals reported either ear pain or tinnitus (one reported both symptoms) and no one displayed all three. Because

dizziness was reported by 23/25 affected individuals, it is not surprising that it is commonly associated with the other prevalent symptoms. For example, dizziness was also reported by all 8 individuals who reported tinnitus, 7/8 individuals who reported hearing loss and 5/7 individuals with ear pain. No patients in the unaffected group had more than one symptom.

Table 1: Symptoms

SYMPTOM	Unaffected group	Affected Group
Dizziness (Yes:No)	0:10 (0%)	23:2 (92%)*
Cognitive (Yes:No)	0:10 (0%)	14:11 (56%)*
Hearing Loss (Yes:No)	0:10 (0%)	8:17 (32%)*
Tinnitus (Yes:No)	0:10 (0%)	8:17 (32%)*
Ear Pain (Yes:No)	0:10 (0%)	7:18 (28%)*
Headache (Yes:No)	2:8 (25%)	6:19 (24%)
MULTIPLE SYMPTOMS		
At least 2 Symptoms (including HA/excluding HA, Yes:No)	0:10/0:10	24: 1/24:1**
At least 3 Symptoms (including HA/excluding HA, Yes:No)	0:10/0:10	16:9 /14:11**

*Significantly difference when compared to asymptomatic group, Fisher exact test, $p < 0.01$

**Both values are significantly different when compared to the asymptomatic group, Fisher exact test, $p < 0.01$

All individuals had a normal ear exam with the exception of mild erythema in the symptomatic ears of 2/7 individuals complaining of ear pain. All of the individuals with dizziness/balance disorders had abnormalities on the qualitative vestibular clinical examination either on spontaneous gaze (spontaneous nystagmus) or on rapid head thrust test (Halmagyi Head Thrust) for more than one passive head

motion frequency. Postural instability was not impacted in this group of individuals nor were significant gait abnormalities identified.

Consistent with the standard of care at our facility for symptomatic patients with potential balance disorder or mild concussion, a more specific set of quantifiable tests was administered to the patients with dizziness to clarify the diagnosis (Table 2). There was a high rate of abnormality (92%) in the subjective visual vertical test ($>3.2^\circ$ deviation from vertical). Eleven individuals with abnormal SVV findings and suspected otolith and semicircular canal-related dysfunction were given rotational vestibulo-ocular reflex tests (horizontal semicircular canal-related function); nine of these patients also received vestibular-evoked myogenic potential testing (otolith-related functional test). The combination of SVV abnormalities and the high prevalence of deficits in both cervical and ocular Vestibular Evoked Myogenic Potential (VEMP) metrics was suggestive of an asymmetric peripheral vestibular pathology affecting the otolithic organs. The rotational chair testing demonstrated aspects of peripheral and central impairment of horizontal semicircular canal pathways, which appeared to be asymmetric.

Table 2: Clinical findings

CLINICAL FINDING (Affected Patients)	Number Tested	Abnormal	Within Normal Limits
Subjective Visual Vertical (SVV)	25	23	2
Chair Rotation HVOR	11	9	2
<i>Central Vestibular Findings</i>		6	5
Antisaccade test	23	12	11

(abnormal error rate)			
Cervical Vestibular Evoked Myogenic Potential) VEMP	9	7	2
Ocular VEMP	9	7	2

The anti-saccade task is an eye movement test related to executive function; it requires a subject to suppress and eye movement to a target and, instead, make an eye movement of the same magnitude in the opposite direction. The high prevalence of abnormal findings was consistent with published findings for a population with the diagnosis of acute mild concussion ^{1,2}.

A subset of nine individuals with specific complaints was referred for a cognitive evaluation. (Figure 3) Most commonly reported neurobehavioral complaints included decreased clarity of thought or “cognitive fog”, inattention, problems retrieving information on demand, especially under distracting conditions, and increased irritability and anxiety as well as overall greater difficulty regulating emotion. Formal neuropsychological testing using a comprehensive battery of tests confirmed these complaints. Decrements were observed in these individuals on measures of verbal fluency, working memory and sustained attention/vigilance, complex auditory processing requiring the ability to discriminate select stimuli from background noise, grip strength, and organizing sequential material during increasingly high levels of cognitive load. Although all individuals reported emotional distress, half formally endorsed depression and anxiety symptoms on self-report questionnaires.

Table 3 Cognitive/Neuropsychological findings

Case #	Premorbid estimate of intellect	Subjective complaints	Neuropsychological Findings
1	NART=114; High Average	<ul style="list-style-type: none"> • Forgetfulness • Mental fog/Slow performance • Difficulty with complex attention • Reduced motivation 	<ul style="list-style-type: none"> • Diminished working memory • Slowed processing speed • Inefficient verbal learning • Reduced verbal fluency • Weak grip strength
2	NART=114; High Average	<ul style="list-style-type: none"> • Forgetfulness • Poor concentration/planning difficulty • Difficulty retrieving words • Mood swings • Increased irritability • Lack of motivation 	<ul style="list-style-type: none"> • Mildly impaired verbal learning and memory • Mild attentional problems • Reduced word finding • Mild depression
3	NART=117; High Average	<ul style="list-style-type: none"> • Slower processing • Difficulty multi-tasking • Difficulty retrieving words • Greater level of effort required to complete simple tasks 	<ul style="list-style-type: none"> • Reduced speed of processing • Weak grip strength • Diminished sustained attention/ problems sustaining mental set • Difficulty making rapid visual comparisons
4	Average	<ul style="list-style-type: none"> • Slower processing • Attentional problems 	<ul style="list-style-type: none"> • Slow processing speed
5	NART=117; High Average	<ul style="list-style-type: none"> • Slower processing • Difficulty concentrating • Difficulty multitasking • Feeling confused • Irritability 	<ul style="list-style-type: none"> • Reduced ability to focus in the face of competing stimuli • Episodic memory • Attention • Working memory difficulties • Weak grip strength.
6	NART=106; Average	<ul style="list-style-type: none"> • Forgetfulness • Slower processing • Poor concentration • Word finding difficulties • Indecisiveness • Irritability, increased tearfulness • decreased interest in activities, anxiety & mood swings 	<ul style="list-style-type: none"> • Difficulty with verbal memory • Reduced fine motor speed • Reduced ability to focus in the face of competing stimuli • Poor Grip Strength • Moderate depression • Mild Anxiety and apathy
7	NART=115; High Average	<ul style="list-style-type: none"> • Forgetfulness • Slower processing • Difficulty retrieving words • Mood lability & anxiety 	<ul style="list-style-type: none"> • Decreased visual memory • Reduced verbal fluency • Weak Grip Strength
8	NART=88; Low Average	<ul style="list-style-type: none"> • Forgetfulness • Slower processing • Poor concentration • Difficulties with organization 	<ul style="list-style-type: none"> • Difficulty with simple verbal and visual attention, visual processing • Reduced ability to focus in the

		<ul style="list-style-type: none"> • Difficulty monitoring • Word finding difficulties 	face of competing stimuli <ul style="list-style-type: none"> • Reduced vocabulary • Mild depression
9	Average	<ul style="list-style-type: none"> • Poor concentration 	<ul style="list-style-type: none"> • Slow processing speed • Diminished abstract problem solving

Discussion

In this retrospective review we describe the symptoms and clinical findings in a cohort of individuals who reported neurosensory symptoms after perceiving a loud, high-pitched sound and/or feeling a pressure sensation in a specific location within a room. The source of this sound/pressure sensation has not been determined but all of the affected individuals appear to be connected with U.S. government or the diplomatic services of allied nations. The disorder appears to be fairly specific for those who actually experienced the sound/pressure sensation because no symptoms were reported by others living in the household or by a group in which no one in the household felt any of these phenomena. It is fair to say that one cannot rule out a similar presentation of symptoms in other individuals who have not reported hearing a sound or perceiving the same pressure sensation. However we have not encountered a comparable clinical presentation in individuals who did report either sensation. Hence, the experience of sound and pressure sensations in these locations appears to be a sufficient condition for the appearance of symptoms and clinically abnormal neurosensory findings.

One must exercise considerable caution in the interpretation of a patient's causal attributions for symptoms associated with balance disorders and mTBI, including neuropsychological complaints. Attribution is obvious for overt exposure scenarios like a blast wave exposure or blunt impact to the head. However, if dizziness is due to a covert cause, the attribution is not as likely to be accurate. The dizziness, ear pain and cognitive symptoms are aversive; as in the case of conditioned taste aversion in the presence of nausea and the symptoms may be attributed to irrelevant but novel conditions that merely coincide temporally with the proximate cause. Attribution and misattribution issues for balance disorders and nausea have been reviewed elsewhere ³⁻⁶. More recently, clinical evidence suggests that cognitive deficits in patients with otic capsule dehiscence are resolved by surgical repair ⁷.

The exposure responsible for these findings is unknown. It would be imprudent to exclude any potential sources at this time. For example, perceptions of sound can occur in response to energy exposures that include microwave pulses in the audible ultrasonic range ⁸ or as synesthetic effects to light ⁹. Pulsed microwave stimulation is known to produce ultrasonic cochlear microphonics in guinea pigs ¹⁰. The ultrasonic frequency range is represented at the base of the cochlea ('hook portion') in close proximity to the vestibule. Because sound activation of saccule and utricle produce cervical and ocular VEMPs ¹¹, respectively, it is not inconceivable that resonant energy in that range could affect vestibular function.

The pattern of findings in the symptomatic group of a vestibulopathy combined with other neurosensory findings is strikingly similar to the presentation of individuals with acute sequelae of mild traumatic brain injury following blast exposure or blunt trauma ¹²⁻¹⁵. It does not seem imprudent to speculate that a highly specific unidentified energy exposure, perceived as a sound or pressure, could be producing a mild traumatic brain injury (mTBI) or similar inner ear concussion. It is noteworthy that most of our patients were seen more than 2 weeks after the perceived exposure, which is within a time window for resolution of most symptoms of acute mTBI from blast or blunt trauma. Although it is unknown how many individuals were potentially at risk, the prevalence of individuals presenting with 2 or more symptoms and the SVV abnormalities seems higher than one would expect two weeks after conventional exposures ¹⁶. In addition the low incidence of headaches (around 25%) is unusual as many studies of mTBI show that headache is one of the most common and persistent symptoms ¹⁷⁻¹⁹. Perhaps the most striking clinical feature is the nearly universal evidence of otolithic impairment; such uniformity in symptoms is uncommon in mTBI cases from other sources ^{20,21}.

Conclusion

This retrospective review examines a phenomenon that to date has only been described in a group of diplomats from select courtiers in one location. The preponderance of evidence suggests that symptoms and signs emerge after perception of a loud noise or

pressure field that is very localized. At the current time the objective findings are very similar to findings in mild traumatic brain injury. While manifesting all of the symptoms seen in the conventional heterogeneous spectrum of mTBI this group of individuals does have some unique features. There is an extremely high incidence of objective signs of underlying otolithic abnormalities and asymmetric vestibulopathies. In addition, the group is much more homogenous in presentation than most mTBI populations. Cognitive symptoms such as problems maintaining sustained attention, slower processing speed, difficulty multi-tasking, and word retrieval difficulties are common in mTBI. Emotional symptoms which include irritability, anxiety and depression are also frequently encountered.

Because this injury pattern could present elsewhere, it is important for individuals who care for patients to be aware of the presenting symptoms and signs. Objective, tests of otolithic and vestibular function such as subjective visual vertigo (SVV), vestibular evoked myogenic potentials (VEMPs), and head rotation test (head impulse tests) proved particularly helpful in this population. Based on experience with similar complaints for patients with balance disorders and mTBI, early identification and treatment will likely be the best method for clinical management. It is also extremely important that resources be utilized to determine the source of this pattern of signs and symptoms so that we can better understand the underlying mechanisms and better work to prevent future injuries.

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